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FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
JAISLE, CECILIA M	

ART UNIT	PAPER NUMBER
1624	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,214	MAEKAWA ET AL.	
	Examiner	Art Unit	
	Cecilia M. Jaisle	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,6,9-11,17-21 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *17* is/are allowed.

6)☒ Claim(s) *1-3,5,6,9-11,18-21 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Rejections Under 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5, 6, 9-11, 18-21 and 23 are rejected under 35 U.S.C. 112, paragraph one, while enabling a method of making compounds of Examples 1-379, do not reasonably enable a method to make and use all compounds these claims encompass. The production methods (pages 73-100, *inter alia*) fail to teach commercial availability or how to make all starting materials and intermediates required to prepare all compounds the claims encompass. The specification fails to teach commercial availability or how to make all necessary starting compounds, (II), (III), (I-2), (I-4), (I-5), (V), (VI), (VIII)-(XI), (XIII)-(XVI) and (XIX), required to prepare all compounds the claims encompass. Each described reaction scheme prepares only certain Formula I compounds of the claims. This is particularly true because the claims encompass undefined substituents on A, B, C, R4, R5 and R6 (together or individually). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use, the invention commensurate in scope with these claims.

Because neither the prior art, nor the present specification nor both of them together teach how to prepare all compounds the claims encompass, it follows as a necessary corollary that the method of using all of these compounds is undisclosed.

Unless Applicants can provide reference to all of the necessary starting materials and procedures required to make all compounds encompassed by claims 1-3, 5, 6, 9-11, 18-21 and 23, these claims must be limited to the supporting disclosure.

Applicants' attention is drawn to the Revised Interim Utility and Written Description Guidelines, 66 FR 1092-1099 (2001), emphasizing that "a claimed invention must have a specific and substantial utility." MPEP 2163, *et. seq*. This application's disclosure is insufficient to enable making certain of the compounds of claims based solely on disclosure of the compounds of Examples 1-379, absent disclosure of a valid method of preparing all of the claimed compounds as noted in the paragraph above. The state of the art indicates the requirement for undue experimentation.

Many factors require consideration when determining whether sufficient evidence supports a conclusion that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue." MPEP 2164.01(a). These factors include: (1) the claim breadth; (2) the nature of the invention; (3) the state of the prior art; (4) the level of predictability in the art; (5) the amount of direction provided by the inventor; (6) the presence of working examples; and (7) the quantity of experimentation needed to make the invention based on the content of the disclosure. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)(reversing the PTO's determination that claims directed to methods for detection of hepatitis B surface antigens did not satisfy the enablement requirement). See also *In re Goodman* 29 USPQ2d 2010, 2013 (Fed. Cir. 1993). Application of these factors to the present application supports the determination that the present disclosure fails to satisfy the enablement requirement:

(1) Breadth of claims.

(a) Scope of the compounds. The claims cover potentially thousands of substituted pyrazole compounds in which many of the substituents are undefined.

(b) Scope of the methods of preparing the compounds. The scope of the methods is stated above and below in Point (3) Direction or Guidance. The specification contains insufficient disclosure of the preparation of all claimed compounds. The method scope is discussed above, and the specification does not disclose preparation of all claimed compounds, particularly failing to show the source of the necessary starting materials and intermediates, or the methods of preparation of the required starting materials and intermediates.

In *In re Albrecht, et al.,* 185 USPQ 590, 594 (CCPA 1975), the claimed compounds were rejected for lack of enablement, because the specification failed to show all necessary starting materials required to prepare all claimed compounds. Appellant attempted to rely on a prior US patent (Anderson) to show such starting materials. J. Baldwin confirmed that, when appellant's claims are rejected as non-enabling for failure to show all starting materials needed to prepare their claimed compounds, appellant must show specifically all such starting materials:

> However, we fail to find all of the missing [starting materials] ... necessary to prepare appellants' claimed compounds. ... It is incumbent upon appellants to show where in the Anderson disclosure one of ordinary skill in the art would glean the necessary information required to satisfy the enablement requirement of the first paragraph of 35 USC 112. The Anderson patent specification contains thirty examples and nine columns of text. Appellants have not pointed out precisely where enablement lies in that disclosure. It is incumbent upon appellants to rebut the assertion that their specification is not enabling.

In re Wands, 8 USPQ2d 1400, 1403 (Fed. Cir. 1988) similarly noted the requirement of the availability of biological organisms when they were necessary starting materials to support enablement of the claims:

> A deposit has been held necessary for enablement where the starting materials ... are not readily available to the public. Even when starting materials are available, a deposit has been necessary where it would require undue experimentation to make the ... invention from the starting materials. ... No deposit is necessary if the biological organisms can be obtained from readily available sources or derived from readily available starting materials through routine screening that does not require undue experimentation.

(2) The nature of the invention and predictability in the art: "[T]he scope of enablement varies inversely with the degree of unpredictability of the factors involved" and the ability to make all claimed compounds is considered to be unpredictable because all necessary starting materials and intermediates have not been shown to be available. *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970). In the instant case, the disclosure does not sufficiently address preparation of all claimed compounds.

(3) Direction or Guidance: The specification teaches (pages 73-100, *inter alia*) methods to make certain compounds of claims 1-3, 5, 6, 9-11, 18-21 and 23, but does not teach methods and required starting materials and intermediates necessary to prepare all claimed compounds. Neither the prior art, nor the present specification nor both of them together teach how to prepare all claimed compounds, especially considering the number of position isomers, homologs and further unidentified substituents encompassed thereby.

(4) State of the Prior Art: Formation of compounds is highly species-specific in organic chemistry. Note that the present claims include compounds having undefined

substituents. *Albrecht* and *Wands*, discussed above, stand as evidence of the prior art acknowledgement that unless starting materials to prepare all compounds within the scope of the claims are available, the claims are not enabled. Applicants must show all necessary starting materials or limit the claims accordingly.

(5) Working Examples: The working examples have been fully discussed in Point 3) Direction or Guidance, above. Pharmacological activity in general is unpredictable. In applications involving physiological activity, such as the present,

> The first paragraph of 35 U.S.C. 112 effectively requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.
>
> *Plant Genetic Syst. v. DeKalb Genet.*, 65 USPQ2d 1452, 1456 (Fed. Cir. 2003).

"[T]he scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970).

(6) Skill of those in the art: The state of the art supports that to successfully prepare all compounds within the scope of the claims requires specific individualized disclosure, particularly considering that many of the intended substituents are undefined.

(7) The quantity of experimentation needed: Based on the disclosure content, one skilled in the pharmaceutical arts would have an undue burden to make and use the invention, since the disclosure gives the skilled artisan inadequate guidance regarding making all claimed compounds, as stated above.

Discussion of the above factors demonstrates that the present application insufficiently enables the present claims. In view of claim breath, unpredictability of methods of making the claimed compounds, lack of definition of all compound substitu-

ents, one of ordinary skill in this art would undergo an undue amount of experimentation to make the instantly claimed invention commensurate with the claim scope.

MPEP 2164.01(a) states,

> A conclusion of lack of enablement means that, based on the evidence regarding each of the above [Wands] factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

This is a circumstance where the "specification is evidence of its own inadequacy." *In re Rainer*, 153 USPQ 802, 807. All claimed compounds cannot be willed into existence. *Morton Intern'tl Inc. v. Cardinal Chem. Co.*, 28 USPQ2d 1190 states:

> The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist ... the examples of the '881 patent do not produce the postulated compounds ... [T]here is ... no evidence that such compounds even exist.

The same circumstance appears true here. Applicants must show making and using all claimed compounds or limit the claims accordingly.

Remarks to Response of 06-08-2009

Applicants assert certain case law cited to support this rejection (*In re Wands, In re Fischer, Plant Syst. v. DeKalb Genet.*) relates to biotechnology inventions not applicable to this situation. The above quote from *In re Wands*, 8 USPQ2d 1400, 1403 (Fed. Cir. 1988) is directly relevant to the present situation, where starting materials necessary to enable the invention are not readily available to the public. *In re Fischer* [sic], 149 USPQ 631 (CCPA 1966), relates to dismissal and remand, is truly not relevant to this situation and was not cited in the previous rejection. *Plant Genetic Syst. v. DeK-*

alb Genetics, 65 USPQ2d 1452, 1456 (Fed. Cir. 2003) noted, "To determine whether there is a reasonable correlation between the scope of the claims and the scope of enablement, the degree of predictability of the relevant art may need to be considered."

The specification fails to teach commercial availability or how to make all necessary starting compounds, (II), (III), (I-2), (I-4), (I-5), (V), (VI), (VIII)-(XI), (XIII)-(XVI) and (XIX), required to prepare all compounds the claims encompass, particularly because the claims encompass undefined substituents on A, B, C, R4, R5 and R6. The manner of making such compounds is unpredictable because the identity of their substituents is unknown. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use, the invention commensurate in scope with these claims, because it fails to teach one skilled in the art what possible substituents are on the starting materials for this invention.

Applicants point to various portions of the specification in an attempt to show that preparation of all necessary starting compounds, (II), (III), (I-2), (I-4), (I-5), (V), (VI), (VIII)-(XI), (XIII)-(XVI) and (XIX), required to prepare all compounds of the claims is disclosed. However, none of those passages teach how to prepare starting materials that have all of the substituents encompassed by the claims. The specification further does not teach how all starting materials may be used to prepare all claimed compounds with undefined substituents. For example, at page 77, compound (I-3) is said to be prepared by oxidation of compound (I-2). However, if A, B and/or C of compound (I-3) has a carbonyl substituent, it will oxidize to the corresponding carboxy substituent. Alkenyl substituents will oxidize to vicinal di-hydroxy substituents. Other substituent groups will

similarly be changed during oxidation. When the substituent of a starting material is unknown and undefined, it is not possible to determine what final product will result.

Applicants assert that they have disclosed how to make the starting materials and intermediates. This is manifestly untrue, when the substituents on such starting materials and final products are unknown and undefined.

Claims 20, 21 and 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating a mammal with type 2 diabetes (claim 20), hyperlipidemia (claim 21) or impaired glucose tolerance (claim 23). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification does not provide competent evidence that the instantly disclosed tests are predictive of all uses disclosed and embraced by the claims. Substantiation of utility and its scope is required when utility is "speculative," "sufficiently unusual" or not provided. See *Ex parte Jovanovics, et al.*, 211 USPQ 907, 909 (BPAI 1981). Also, note *Hoffman v. Klaus*, 9 USPQ2d 1657 (BPAI 1988) and *Ex parte Powers*, 220 USPQ 924 (BPAI 1982) regarding types of testing needed to support *in vivo* uses.

Applicants' attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 66 FR 1092-1099 (2001), emphasizing that "a claimed invention must have a specific and substantial utility." See also MPEP 2163, *et. seq.*

This application's disclosure is insufficient to enable the instantly claimed methods. The state of the art indicates the requirement for undue experimentation.

Many factors require consideration when determining whether sufficient evidence supports a conclusion that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue." MPEP 2164.01(a). These factors include: (1) the claim breadth; (2) the nature of the invention; (3) the state of the prior art; (4) the level of predictability in the art; (5) the amount of direction provided by the inventor; (6) the presence of working examples; and (7) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)(reversing the PTO's determination that claims directed to methods for detection of hepatitis B surface antigens did not satisfy the enablement requirement). See also *In re Goodman* 29 USPQ2d 2010, 2013 (Fed. Cir. 1993). Application of these factors to the present application supports the determination that the present disclosure fails to satisfy the enablement requirement:

(1) Breadth of claims.

(a) Scope of the methods. The method claims cover the use of substituted pyrazole compounds and their pharmaceutically acceptable salts.

(b) Scope of the disorders covered. Scope of disorders said to be treated by claimed methods are stated above and further discussed in the previous Office Action.

(2) The nature of the invention and predictability in the art: Therapeutic use of substituted pyrazoles and salts in preventing and treating disorders recited above. It is well established that "the scope of enablement varies inversely with the degree of

unpredictability of the factors involved" and physiological activity is generally considered to be an unpredictable factor. *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970).

(3) Direction or Guidance: That provided is very limited. Dosage range information is meager; it would require extensive experimentation to determine specific dosage for a specific recited disorder, mode of administration and therapeutic regimen. The dosage is generic; the same for many disorders the specification covers. No specific direction or guidance gives a regimen or dosage effective specifically for various types of diseases. No dosage or therapeutic regimen is present to direct the skilled artisan to treat a host suffering from all named disorders.

(4) State of the Prior Art: Kebede, et al., Diabetes 57:2432-2437, 2008 reports research that raises "doubts on the validity of a therapeutic approach based on GPR40 antagonism for the treatment of type 2 diabetes."

Calkin, et al., Nephrol. Dial. Transplant. (2006), 21:2399-2405, points to the need for further research:

> ...[T]he PPAR-alpha agonist, gemfibrozil, the PPAR-gamma, rosiglitazone and the PPAR-alpha/gamma co-agonist, compound 3q, have equivalent renoprotective actions in experimental diabetes, over and above effects on plasma, glucose, blood pressure or lipid levels. This finding is consistent with the important role of the PPAR signaling system in diabetic complications. Moreover, these benefits correlate with the direct antiatherogenic effects of PPAR agonists observed in the diabetic vasculature. The clinical relevance of this finding remains to be established, given the negative effects of the dual agonist, muraglitazar in patients with diabetes and equivocal outcomes with side effects observed in the recent FIELD and proACTIVE studies.

Wieser, et al., PPAR Res. 2008; 2008: 527048, reports alarming findings:

> Ongoing basic studies have elucidated the metabolic, antiinflammatory, and angiogenic benefits of PPAR$\alpha/\beta/\delta$ and PPAR$\gamma/\beta/\delta$ dual agonists and

> PPAR pan agonists for treatment purposes. However, some experimental and clinical data have uncovered unfortunate side effects of PPAR ligands, including cancer progression and increased cardiac event rates. New generations of PPAR modulators are under development and these promise to be more receptor-specific, and hopefully will activate only a specific subset of target genes and metabolic pathways to reduce untoward side effects. The potential role of PPARs in regulation of inflammation and angiogenesis is intriguing and warrants further studies. We submit that PPAR agonists may become beneficial drugs for pregnancy-specific diseases, once their risks have been fully evaluated.

Ability of claimed methods to treat all disorders asserted above remains open to proof. A person skilled in this art would encounter undue experimentation.

(5) Working Examples: The disclosure fails to correlate the test results in the specification to the treatments construed by the claims. The specification merely prophesies that the methods will treat prevent all disorders mentioned above.

The specification states that the methods treat all claimed disorders, for which Applicants provide insufficient evidence. Applicants have not provided competent evidence of known tests highly predictive for all disorders embraced by the claim language for the intended host. Pharmacological activity in general is unpredictable. In applications involving physiological activity, such as the present,

> "The first paragraph of 35 U.S.C. 112 effectively requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art."

Plant Genetic Syst. v. DeKalb Genetics, 65 USPQ2d 1452, 1456 (Fed. Cir. 2003). "[T]he scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." *In re Fisher*, 166 USPQ 18 (CCPA 1970).

(6) Skill of those in the art: See the discussion above of Kebede, Calkin and Wieser. The state of the art supports that successful treatment and prevention of all disorders recited is a subject for further investigation.

(7) The quantity of experimentation needed: Based on the disclosure content, to use the invention would place an undue burden on one skilled in the pharmaceutical arts, since the disclosure gives the skilled artisan inadequate guidance regarding pharmaceutical use, for the reasons stated above.

The discussion of the above factors demonstrates that the present application sufficiently lacks enablement of the present claims. In view of the breath of the claims, the pharmaceutical nature of the invention, the unpredictability of relationship between 5-HT2 receptor antagonist activity and treatment and prevention of all disorders, one of ordinary skill in this art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP 2164.01(a) states,

> A conclusion of lack of enablement means that, based on the evidence regarding each of the above [Wand] factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Response to Remarks of 01/21/2009

Applicants point to various passages in the specification as supposedly teaching how to use the present method claims. However, Applicants are silent on the above-cited articles that cast doubt on the validity of a therapeutic approach based on GPR40 or PPAR antagonism for treatment of type 2 diabetes, hyperlipidemia and or impaired glucose tolerance.

Applicants assert Kebede is not relevant as the claim based on GPR4-antagonism has been canceled. However, GPR4-antagonism by the present compounds is one basis for Applicants' hypothesis that the present compounds will treat type-2 diabetes, a hypothesis that Kebede does not support.

Wieser confirms that experimental and clinical data uncovered PPAR ligand side effects, including progression of cancer, increased cardiac event rates, and requires further evaluation before they can become potential drugs.

Calkin reports that the clinical relevance of their findings must still be established, particularly in light of the negative effects of the dual agonist, muraglitazar, in diabetic patients and equivocal outcomes with side effects observed in the recent FIELD and proACTIVE studies.

Regarding muraglitazar, a Bristol-Myers Squibb PPAR agonist, its further development was discontinued as of May 2006. Data on muraglitazar is relatively less due to recent introduction of this agent. One double-blind randomized clinical trial comparing muraglitazar and pioglitazone found that effects of the former were favorable in terms of HDL-C increase, decrease in total cholesterol, apolipoprotein B, triglycerides and a greater reduction in HbA1c ($P<0.0001$ for all

comparisons). However, the muraglitazar group had a higher all-cause mortality, greater incidence of edema and heart failure and more weight gain compared to the pioglitazone group. A meta-analysis of the phase 2 and 3 clinical trials of muraglitazar revealed that it was associated with a greater incidence of myocardial infarction, stroke, transient ischemic attacks and congestive heart failure when compared to placebo or pioglitazone. Wikipedia, Muraglitazar, updated Dec. 26, 2008, <http://en.wikipedia.org/wiki/Muraglitazar>, downloaded 3/8/2009.

The teachings of Iwatsuka, Kimura, Alberts and Depres (cited by Applicants) have been carefully considered, but they are not seen to overcome more recent and relevant teachings of Kebede, Calkin and Wieser (cited by the examiner), and the discussion of muraglitazar, all considered in detail above.

Anantanarayan describes a compound falling within the original claimed compounds and methods genus, but is not described as evidencing efficacy for treating a mammal with type 2 diabetes, hyperlipidemia or impaired glucose tolerance. Though Applicants have amended the claims to avoid Anantanarayan, this reference calls into question whether all claimed compounds evidence such properties, especially considering claimed compounds with unidentified substituents.

The record fails to establish that the skilled practitioner would be able to use the present methods as broadly as claimed without having to undergo extensive inventive research.

Sitrick v. Dreamworks LLC, 85 USPQ2d 1826, 1830 (Fed. Cir. 2008) decided that a claim is not enabled when the claim covers multiple embodiments but the specification

fails to enable all of the embodiments. "Because the asserted claims are broad enough to cover both [embodiments], the [specification] must enable both embodiments." Here, the claims at issue cover many methods and do not enable all of them.

Automotive Tech. Int'l. v. BMW of N. America, Inc., 84 USPQ2d 1108, 1116 (Fed. Cir. 2007) decided that a claim is not enabled when the claim covers multiple embodiments but the specification fails to enable one of the embodiments. "Thus, in order to fulfill the enablement requirement, the specification must enable the full scope of the claims that includes both [embodiments], which the specification fails to do." Here, the claims at issue cover many methods and do not enable all of them.

Applicants make no comment on these two recently decided cases, which are seen to be very close to the facts of this situation.

Rejections Under 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

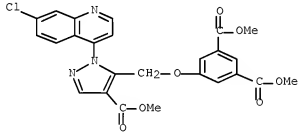
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

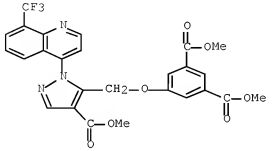
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 9 and 11 are rejected under 35 U.S.C. 103(a) as unpatentable over WO 2001 002385, Emeric, et al., published Jun. 29, 2000 (already of record), describing RN 318492-52-3, 1,3-Benzenedicarboxylic acid, 5-[[1-(7-chloro-4-quinolinyl)-4-(methoxycarbonyl)-1H-pyrazol-5-yl]methoxy]-, dimethyl ester,



and

RN 318492-66-9, 1,3-Benzenedicarboxylic acid, 5-[[4-(methoxycarbonyl)-1-[8-(trifluoromethyl)-4-quinolinyl]-1H-pyrazol-5-yl]methoxy]-, dimethyl ester,



as agrochemical fungicides. The present claims recite methylene homologs of Emeric compounds, where Xa is a bond, Ya is CH2, Xb is O and Yb is a bond, which compounds are obvious for the Emeric utility.

One of ordinary skill in the art would have found it obvious when the present invention was made to modify Emeric compounds to prepare their structural homologs. One of ordinary skill in the art would have been motivated to prepare the instantly claimed compounds because such structural homologs are expected to possess similar properties. It has been held that compounds that are structurally homologous to prior art compounds are *prima facie* obvious, absent a showing of unexpected results.

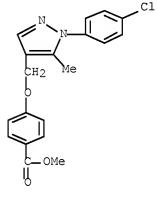
> An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties.

In re Payne, 203 USPQ 245, 254 (CCPA 1979). See also *In re Papesch*, 137 USPQ 43 (CCPA 1963) and *In re Dillon*, 16 USPQ2d 1897 (Fed. Cir. 1991) (discussed in MPEP § 2144) for an extensive case law review pertaining to obviousness based on close structural chemical compound similarity. See also MPEP § 2144.08, ¶ II.A.4(c). Compounds that are homologs (compounds differing regularly by successive addition of the same chemical group, e.g., by CH3- groups), as here, are generally of sufficiently

close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 195 USPQ 426 (CCPA 1977).

Claims 1-3, 6, 9 and 11 are rejected under 35 U.S.C. 103(a) as unpatentable over JP 11130753, Kitaide, et al., published Oct. 31, 1997 (already of record), describing

RN 225930-55-2, Benzoic acid, 4-[[1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-yl]methoxy]-, methyl ester,



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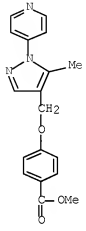
RN 225930-59-6, Benzoic acid, 4-[[5-methyl-1-(4-pyridinyl)-1H-pyrazol-4-yl]methoxy]-, methyl ester,



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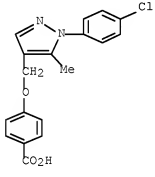
RN 225930-67-6, Benzoic acid, 4-[[1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-yl]methoxy]-, methyl ester,



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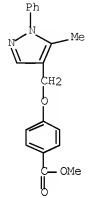
RN 225930-68-7, Benzoic acid, 4-[(5-methyl-1-phenyl-1H-pyrazol-4-yl)methoxy]-, methyl ester,



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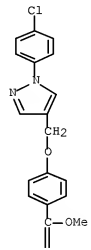
RN 225930-69-8, Benzoic acid, 4-[[1-(4-chlorophenyl)-1H-pyrazol-4-yl]methoxy]-, methyl ester,

PAGE 1-A



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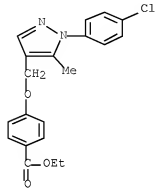
RN 225930-70-1, Benzoic acid, 4-[[1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-yl]methoxy]-, ethyl ester,



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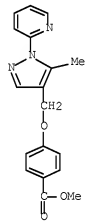
RN 225930-72-3, Benzoic acid, 4-[[5-methyl-1-(2-pyridinyl)-1H-pyrazol-4-yl]methoxy]-, methyl ester,



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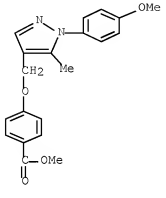
RN 225930-73-4, Benzoic acid, 4-[[1-(4-methoxyphenyl)-5-methyl-1H-pyrazol-4-yl]methoxy]-, methyl ester,



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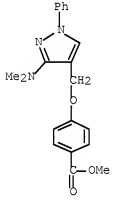
RN 225930-74-5, Benzoic acid, 4-[[3-(dimethylamino)-1-phenyl-1H-pyrazol-4-yl]methoxy]-, methyl ester,



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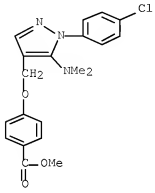
RN 225930-75-6, Benzoic acid, 4-[[1-(4-chlorophenyl)-5-(dimethylamino)-1H-pyrazol-4-yl]methoxy]-, methyl ester,



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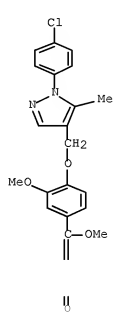
RN 225930-76-7, Benzoic acid, 4-[[1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-yl]methoxy]-3-methoxy-, methyl ester,



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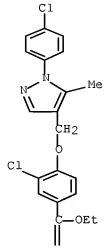
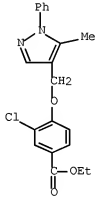
RN 225930-77-8, Benzoic acid, 3-chloro-4-[[1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-yl]methoxy]-, ethyl ester,

PAGE 1-A



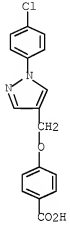
PAGE 2-A

RN 225930-78-9, Benzoic acid, 3-chloro-4-[(5-methyl-1-phenyl-1H-pyrazol-4-



yl)methoxy]-, ethyl ester,

RN 225930-80-3, Benzoic acid, 4-[[1-(4-chlorophenyl)-1H-pyrazol-4-yl]methoxy]-,



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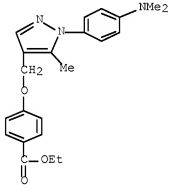
RN 225930-81-4, Benzoic acid, 4-[[1-[4-(dimethylamino)phenyl]-5-methyl-1H-pyrazol-4-yl]methoxy]-, ethyl ester,



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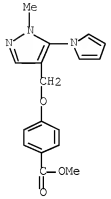
RN 225930-82-5, Benzoic acid, 4-[[1-methyl-5-(1H-pyrrol-1-yl)-1H-pyrazol-4-yl]methoxy]-, methyl ester,



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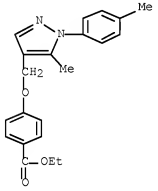
RN 225930-83-6, Benzoic acid, 4-[[5-methyl-1-(4-methylphenyl)-1H-pyrazol-4-yl]methoxy]-, ethyl ester,



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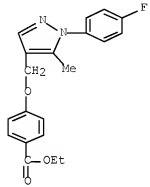
RN 225930-84-7, Benzoic acid, 4-[[1-(4-fluorophenyl)-5-methyl-1H-pyrazol-4-yl]methoxy]-, ethyl ester,



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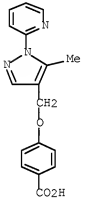
RN 225930-86-9, Benzoic acid, 4-[[5-methyl-1-(2-pyridinyl)-1H-pyrazol-4-yl]methoxy]-,



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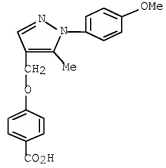
RN 225930-87-0, Benzoic acid, 4-[[1-(4-methoxyphenyl)-5-methyl-1H-pyrazol-4-yl]methoxy]-,



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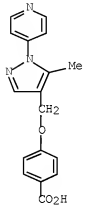
RN 225930-88-1, Benzoic acid, 4-[[5-methyl-1-(4-pyridinyl)-1H-pyrazol-4-yl]methoxy]-,



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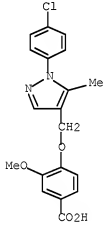
RN 225930-90-5, Benzoic acid, 4-[[1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-yl]methoxy]-3-methoxy-,



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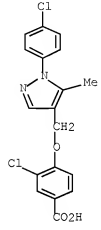
RN 225930-91-6, Benzoic acid, 3-chloro-4-[[1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-yl]methoxy]-,



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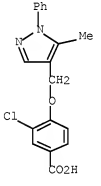
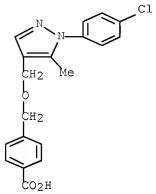
RN 225930-92-7, Benzoic acid, 3-chloro-4-[(5-methyl-1-phenyl-1H-pyrazol-4-yl)methoxy]-,



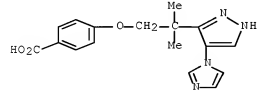
, and

RN 225930-95-0, Benzoic acid, 4-[[[1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-yl]methoxy]methyl]-,

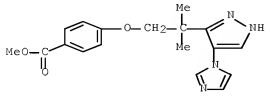


, as lipid formation inhibitors. The present claims recite CH2 homologs of the Kitaide compounds, where Xa is a bond, Ya is CH2, Xb is O and Yb is a bond, which compounds are obvious for the Kitaide utility. See the discussion above of the obviousness of methylene homologs, repeated here as equally pertinent.

Claims 1, 2, 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elbe, et al., DE 3300795, published Jan. 12, 1983 (already of record), describing RN 92782-09-7, Benzoic acid, 4-[2-[4-(1H-imidazol-1-yl)-1H-pyrazol-3-yl]-2-methylpropoxy]-



, and RN 92782-16-6, Benzoic acid, 4-[2-[4-(1H-imidazol-1-yl)-1H-pyrazol-3-yl]-2-methylpropoxy]-, methyl ester,



, with antithromboembolic action. The present claims recite CH2 homologs of the Elbe compounds, where Xa is a bond, Ya is CH2, Xb is O and Yb is a bond, which compounds are obvious for the Elbe utility. See the discussion above of the obviousness of CH2 homologs, repeated here as equally pertinent.

Allowed Claim

Claim 17 is allowed. Here is an examiner's statement of reasons for allowance.

Anantanarayan, Elbe, Kitaide and Emeric and other prior art cited against claims during this prosecution all describe certain substituted pyrazole compounds, however, claim 17 compounds have a particular substitution pattern neither anticipated nor rendered obvious thereby. In addition, none of the prior art of record either anticipates or renders obvious claim 17 compounds, whether taken alone or in any combination.

Conclusion

Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cecilia M. Jaisle whose telephone number is 571-272-9931. The examiner can normally be reached on Monday through Friday; 8:30 am through 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. If you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cecilia M. Jaisle/
Patent Examiner, AU 1624

/James O. Wilson/
Supervisory Patent Examiner, AU 1624